

REVIEW ARTICLE NUMBER 33

NATURAL BICOUMARINS

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Key Word Index—Natural bicoumarin; spectral data, structure, synthesis.

Abstract—Natural bicoumarins isolated from both plant sources as well as microorganisms have been catalogued and their spectral properties compiled.

The coumarins are a large group of naturally occurring oxygen heterocycles, *ca* 1000 of them having been isolated until now [1]. The bicoumarins are a comparatively new group among them and only *ca* 29 have been encountered in nature so far. The first of this series of compounds to be isolated was dicoumarol [2] in 1941.

The bicoumarins isolated from plant sources fall into the following categories: (i) where the two coumarin units are linked at C3–C3' through a methylene group, i.e. dicoumarol [2, 3], gerberinol [4, 5]; (ii) the two coumarin units are linked by an ether bridge, i.e. daphnoretin [6–36], Gunasekera *et al.*, unpublished results, demethyl-daphnoretin [37], acetyldaphnoretin [38], daphnorin [17, 27, 39], candicanin [40], lasiocephalin [41–43], fatagarin [44], oreojasmin [44], edgeworthin [22]; (iii) the third type in which the two coumarin systems are attached through a carbon–carbon bond, i.e. bicoumol [45], bhubaneswin [46], matsukaze lactone [46, 47], kotanin [48–50], desmethylkotanin [48], orlandin [50], euphorbetin [51–53], isoeuphorbetin [52, 54], ipomopsin [55]; (iv) where the two coumarin units are linked through a C-10 alkyl residue (monoterpene unit), i.e. thamnusin [56–58], phebalin [59], isothamnusin A [60], isothamnusin B [60], toddasin/mexolide [61, 62] and (v) where the two coumarin nuclei are linked through 7-methyljuglone unit as in ismailin [63, 64]. In addition, there are two other bicoumarins where the two coumarin units are linked by an ether bridge at C7–C7' as well as a C–C bond at C8–C8' as in gnidicoumarin [65] and in lasioerin [66] the corresponding linkages are through C7–C7' and C6–C6' respectively. In the only naturally occurring bicoumarin-rhamnoside, eriocephalose [67] the coumarin nuclei are linked through an ether bridge C4–C7' and the C–C bond is at C3–C8'.

This review is concerned with the literature on all bicoumarins reported up to the middle of 1986 (*Chem. Abst.* 104) and is presented principally in tabular form. The available spectral data for each individual member is incorporated where UV data are in nm with log ϵ values in parenthesis, the IR data in cm^{-1} and NMR chemical shifts are in δ units. Mass spectral mass numbers are followed in parenthesis by relative abundance of ions,

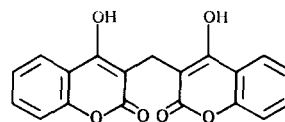
Table 1. Alphabetical list of bicoumarins

No.	Name	No.	Name
5.	Acetyldaphnoretin	27.	Gnidicoumarin
13.	Bhubaneswin	20.	Ipomopsin
12.	Bicoumol	26.	Ismailin
7.	Candicanin	19.	Isoeuphorbetin
3.	Daphnoretin	23.	Isothamnusin A
6.	Daphnorin	24.	Isothamnusin B
4.	Demethyl-daphnoretin	15.	Kotanin
16.	Desmethylkotanin	8.	Lasiocephalin
1.	Dicoumarol	28.	Lasioerin
11.	Edgeworthin	14.	Matsukazelactone
29.	Eriocephalose	10.	Oreojasmin
18.	Euphorbetin	17.	Orlandin
9.	Fatagarin	22.	Phebalin
2.	Gerberinol	21.	Thamnusin
		25.	Toddasin/Mexolide

wherever they have been reported in the original literature.

The detailed list of bicoumarins in alphabetical order is given in Table 1 and their occurrences in plants/microorganisms are given in Table 2.

1. Dicoumarol



$\text{C}_{19}\text{H}_{12}\text{O}_6$: 336.0633.

Mp: 288–289° [2].

Source: *Melilotus alba* (sweet clover hay) [2].

Derivatives: dimethyl ether (168–170°), diacetate (250–252°) [2].

Synthesis [3].

Table 2. Occurrence of bicoumarins in plant sources/micro-organisms

Compositae	<i>Thamnosma</i>
<i>Gerbera</i>	Thamnolin (21)
Gerberinol (2)	<i>Toddalia</i>
Euphorbiaceae	Toddasin/Mexolide (25)
<i>Euphorbia</i>	<i>Zanthoxylum</i>
Euphorbetin (18)	Thamnolin (21)
Isoeuphorbetin (19)	Thymelaeaceae
Ebenaceae	<i>Daphne</i>
<i>Diospyros</i>	Daphnoretin (3)
Ismailin (26)	Demethyl daphnoretin (4)
Leguminosae	Daphnorin (6)
Coronilla	<i>Daphnopsis</i>
Daphnoretin (3)	Daphnoretin (3)
<i>Melilotus</i>	Acetyl daphnoretin (5)
Dicoumarol (1)	Edgeworthin (11)
<i>Trifolium</i>	<i>Gnindia</i>
Daphnoretin (3)	Gnidicoumarin (27)
Bicoumol (12)	<i>Lasiosiphon</i>
Polimoniaceae	Lasiocephalin (8)
<i>Ipomopsis</i>	Lasioerin
Ipomopsin (20)	Erioccephalolide (29)
Rutaceae	<i>Peddiea</i>
<i>Boenninghausenia</i>	Daphnoretin (3)
Daphnoretin (3)	<i>Thymelaea</i>
Matsukaze lactone (14)	Daphnoretin (3)
Bhubaneswin (13)	Daphnorin (6)
<i>Muraya</i>	<i>Wikstroemia</i>
Todasin/Mexolide (25)	Daphnoretin (3)
<i>Phebaium</i>	Umbelliferae
Phebalin (22)	<i>Heracleum</i>
<i>Ruta</i>	Candicanin (7)
Daphnoretin (3)	Micro-organism
Fatagarin (9)	<i>Aspergillus</i>
Oreojasmin (10)	Kotanin (15)
Daphnorin (6)	Desmethylkotanin (16)
Isothamnolin A (23)	Orlandin (17)
Isothamnolin B (24)	

C₃₂H₂₈O₁₀: 572.1682.Mp: 153° (C₆H₆-EtOAc) [40].

UV: (EtOH) 300 (4.36) [40].

IR: (KBr) 3265, 1725, 1100, 1030 [40].

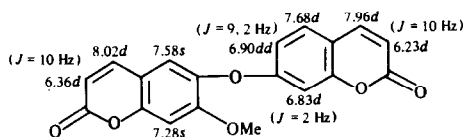
¹H NMR: (CDCl₃) [40].

MS: II/614, 413, 329, 269, 201 [40].

Source: *Heracleum candicans* [40].

Derivatives: acetate, heraclenol (117–118°), xanthotoxol (252–253°) [40].

8. Lasiocephalin

C₁₉H₁₂O₆: 336.0633.MP: 217–218° (CH₂Cl₂-MeOH) [43].

UV: (EtOH) 296 (sh) (4.22), 325 (4.45) [43].

IR: (KBr) 1725, 1630 [43].

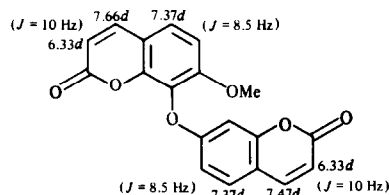
¹H NMR: (DMSO-*d*₆) [43].

MS: 336 (100), 308 (60), 293 (40), 280 (30), 265 (60), 249 (20), 237 (45), 159 (50), 89 (60) [43].

Source: *Lasiosiphon eriocephalus* Decne [41, 42].

Synthesis [43].

9. Fatagarin



H-6', H-8' 6.75–7.10 (2H, m)

C₂₅H₂₂O₁₂: 514.1111.Mp: 202–204° (MeOH-H₂O) [17].[α]_D²⁰: -78° (H₂O; c 0.6) [17].

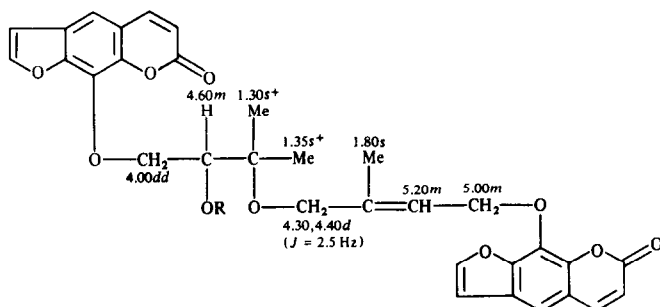
UV: 224 (4.34), 260 (3.90), 325 (4.31), 339 (4.34) [17].

IR: 1720, 1610, 1500, 1270 [17].

Sources: *Daphne mezereum* [17], *Ruta graveolens* [4].*Thymelaea hirsuta* [27].

Derivative: daphnoretin (244°) [17].

7. Candicanin



1 R = H

2 R = Ac

C₁₉H₁₂O₆: 336.0633.

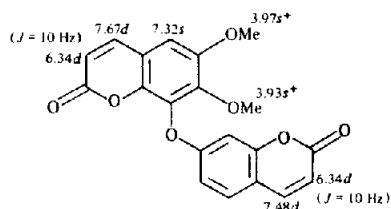
MP: 233–234° [44].

UV: (EtOH) 207 (4.92), 213 sh (4.69), 228 sh (4.47), 255 sh (4.10), 302 (4.40), 332 (4.72) [44].

¹H NMR: (CDCl₃) [44].Source: *Ruta oreojasma* [44].

Derivatives: 7-hydroxy coumarin (232°) and 7-methoxy coumarin (117°) [44].

10. Oreojasmin



Ar-H 6.80–7.10 (3H)

 $C_{20}H_{14}O_7$: 366.0739.

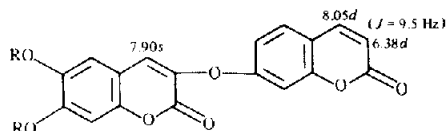
Mp: 238–239° [44].

UV: (EtOH) 208 (4.91), 229 sh (4.54), 284 (4.19), 298 sh (4.30), 327 sh (4.48), 344 (4.50) [44].

 1H NMR: ($CDCl_3$) [44].Source: *Ruta oreojasma* [44].

Derivatives: 7-hydroxy coumarin (232°), 6,7-dimethoxy coumarin (144–146°) [44].

11. Edgeworthin



Ar-H 7.08–7.80 (5H), OAc 2.36 (6H)

1 R = H

2 R = Ac (1H NMR taken) $C_{18}H_{10}O_7$: 338.0426.

Mp: 280–282° (THF) [22].

UV: 200 (4.84), 290 (4.10), 321 (4.22) [22].

IR: 3350, 1690, 1610 [22].

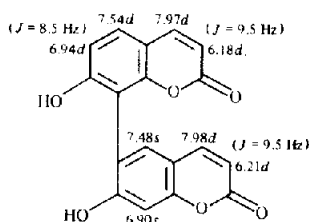
 1H NMR: ($DMSO-d_6$) [22].

MS: 338, 310, 282, 165, 145, 117, 89 [22].

Source: *Edgeworthia gardneri* [22].

Derivatives: dimethyl ether (231°), diacetate (189°, naturally occurring) [22].

12. Bicoumol

 $C_{18}H_{10}O_6$: 322.0477.Mp: 293–294° (EtOH– Me_2CO) [45].

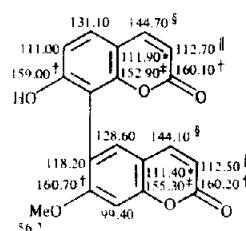
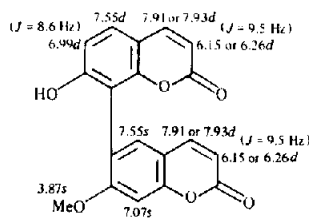
UV: (EtOH) 258 (sh), 328 [45].

IR: 3370, 3270, 1709 [45].

 1H NMR: ($DMSO-d_6$) [45].Source: *Trifolium repens* (Ladino clover) [45].

Derivatives: dimethyl ether (266.5–267.5°), diacetate (228.5–229.5°) [45].

13. Bhubaneswin

 $C_{19}H_{12}O_6$: 336.0633.Mp: 320° ($Me_2CO-CHCl_3$) [46].

UV: (MeOH) 211 (4.08), 326 (3.95) [46].

IR: (KBr) 3250, 1725, 1680, 1600, 1205, 1145, 1100, 1005, 910, 825, [46].

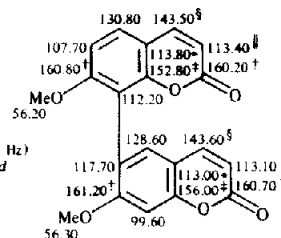
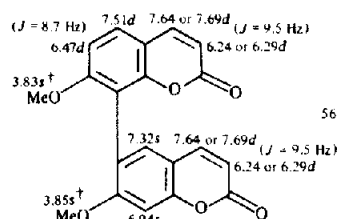
 1H NMR: (CD_3) $_2CO$ [46]. ^{13}C NMR: ($DMSO-d_6$) [46].

MS: 336 (100), 319 (12), 305 (35), 291 (18), 277 (13), 265 (17), 249 (11), 163 (7), 152 (11), [46].

Source: *Boenninghausenia albiflora*, Reichb. ex Meissner [46].

Derivatives: acetate (275°), methyl ether (266–267°) [46].

14. Matsukaze lactone

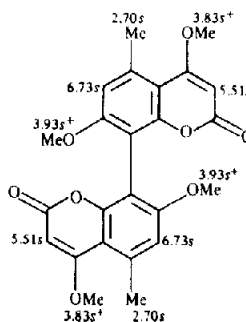
 $C_{20}H_{14}O_6$: 350.0790.Mp: 267–268° (Me_2CO) [47].

UV: (EtOH) 220 (4.37), 257 (4.02), 326 (4.44) [47].

IR: (KBr) 1724, 1605, 1566, 1500, 1374, 1250, 1100, 831, 820 [47].

 1H NMR: ($CDCl_3$) [46]. ^{13}C NMR: ($CDCl_3$) [46].Sources: *Boenninghausenia albiflora*, Reichb. ex Meissner [46, 47].*Boenninghausenia japonica* (Sieb) Nakai [8].

15. Kotanin



$C_{24}H_{22}O_8$: 438.1314.

$[\alpha]_D^{25}$: +33.1° ($CHCl_3$; c 1.75) [48].

Mp: 315° ($CHCl_3$ -MeOH) [48].

UV: (EtOH) 235 (4.37), 250 (4.09), 290 (4.40), 307 (4.46), 316 (4.39) [48].

IR: ($CHCl_3$) 3000, 2930, 2860, 1700, 1615, 1590, 960 [48].

1H NMR: ($CDCl_3$) [48].

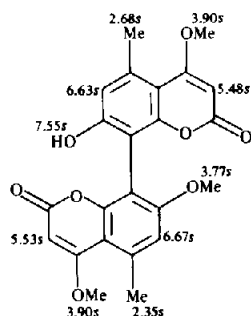
MS: 438 [48].

Sources: *Aspergillus glaucus* [48].

Aspergillus clavatus [49].

Synthesis: [48, 50].

16. Desmethyl kotanin



$C_{23}H_{20}O_8$: 424.1158.

$[\alpha]_D^{25}$: -13.3° ($CHCl_3$; c 1.20) [48].

Mp: 315 ($CHCl_3$ -hexane) [48].

UV: (EtOH) 230 (4.35), 294 (4.35), 308 (4.45), 315 (4.38) [48].

IR: ($CHCl_3$) 3000, 2950, 1700, 1618, 1590, 1460 [48].

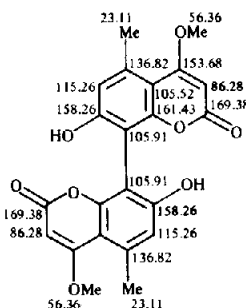
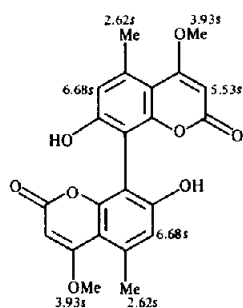
1H NMR: ($CDCl_3$) [48].

MS: 424 [48].

Source: *Aspergillus glaucus* [48].

Derivative: Methyl ether (315°) [48].

17. Orlandin



$C_{22}H_{18}O_8$: 410.1002.

Mp: 285° [50].

UV: (EtOH) 311 (4.47), 321 (sh), 4.40 [50].

IR: (KBr) 3300-3200 (br), 1675, 1605, 1590, 1560, 1450, 1360, 1325, 1262, 1205, 1132, 1105, 1087, 1035, 1015, 1002, 970, 795, 785 [50].

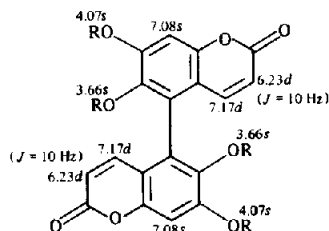
1H NMR: ($DMSO-d_6$) [50].

^{13}C NMR: ($DMSO-d_6$) [50].

MS: 410 [50].

Source: *Aspergillus niger* [50].

18. Euphorbetin



1 R = H

2 R = Me (1H NMR/MS taken)

$C_{18}H_{10}O_8$: 354.0375.

Mp: 320 [51].

IR: (Nujol) 3250, 1665, 1600 [51].

1H NMR: ($CDCl_3$) [51].

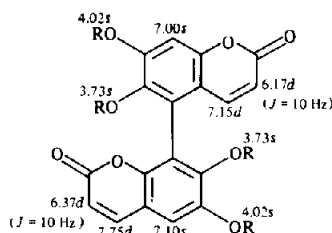
MS: II/410 (100), 395 (7), 379 (50), 364 (82), 349 (13), 336 (31), 321 (16), 308 (14), 293 (21), 205 (35) [51].

Source: *Euphorbia lathyris* L. [51].

Derivatives: tetracetate (235-237°), tetramethyl ether (230-232°) [51].

Synthesis: [52, 53].

19. Isoeuphorbetin



1 R = H

2 R = Me

$C_{18}H_{10}O_8$: 354.0375.

Mp: 300° [54].

IR: (KBr) 3250, 1660-1680, 1600, 1550, [54].

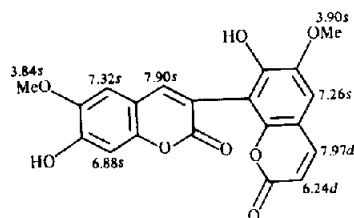
1H NMR: ($CDCl_3$) [54].

Source: *Euphorbia lathyris* L. [54].

Derivative: tetramethyl ether (197-199°) [54].

Synthesis: [52].

20. Ipomopsin



Source: *Lasiosiphon eriocephalus* [67].

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